



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/928,227	08/09/2001	Michael J. Mahan	220002060725	7979

25226 7590 08/27/2003

MORRISON & FOERSTER LLP
755 PAGE MILL RD
PALO ALTO, CA 94304-1018

EXAMINER

PORTNER, VIRGINIA ALLEN

ART UNIT	PAPER NUMBER
----------	--------------

1645

DATE MAILED: 08/27/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/928,227

Applicant(s)

MAHAN ET AL.

Examiner

Ginny Portner

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 09 August 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-46 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-46 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 11,13.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

Art Unit: 1645

DETAILED ACTION

Claims 1-46 are pending.

Priority

1. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Information Disclosure Statement

2. The information disclosure statement filed May 13, 2002 and July 8, 2002 have been considered as to the merits.

Drawings

3. The Brief Description of Figures 6 and 7 should refer to each embodiment by frame. For example 6A and 6B or 7A-7D. Clarification of the figures and the Brief Description of the drawings is requested.

Specification

4. The disclosure is objected to because of the following informalities:
 - a. At page 17, paragraph 0067 an image of a "hand" is recited. What is the hand intended to define?
 - b. At page 18, paragraph 0068 an image of a "hand" is recited. What is the hand intended to define?
 - c. At page 70, Table 1, just before paragraph 0248 an image of a "lined page" is recited. What is this image intended to define? Appropriate correction is requested.

Claim Rejections - 35 U.S.C. § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

Art Unit: 1645

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 24-33, 34-46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 24-33 and 34-46 are directed to method of treating a bacterial infection, and compositions that comprise a compound that alters native DNA adenine methylase activity; the method comprising the step of "administering" an "active agent".

The structure of the agents administered and which is contained in the claimed compositions have been claimed based upon a biological function and not by structure.

At page 53, of the instant specification, screening assays are proposed as means for identifying agents with the recited biological activity, but no specific molecules which evidence specific DNA methyltransferase activity altering structures which correlate with the altering of biological activity which can be administered to a living subject infected with a bacteria are set forth, and said agent function as a therapeutic agent in the process of eradicating bacterial infection.

Art Unit: 1645

The specification proposes to identify, isolate and determine what agents have the recited biological function for treating bacterial infection. What has not been described has not been enabled. The person of skill in the art could not make and use an agent based only upon biological function. The claimed invention is not enable as it has not been described.

8. Claims 24-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of stimulating an immune response against a pathogen, does not reasonably provide enablement for stimulation of a protective immune response that can prevent or treat infection caused by the pathogen when dam gene activity is altered. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant specification and the claims are directed to methods of eliciting a protective immune response against infection in any pathogen through administering a bacteria with a mutation that alters DNA adenine methylase activity and reduces a symptom.

The specification fails to teach how to formulate and use the claimed vaccines. The term "vaccine" encompasses the ability of the specific antigen to induce protective immunity to infection or disease induction.

The dose is any amount to induce an immune response and the route of administration is any route to reduce a single symptom. The specification does not describe mutations that are effective to attenuate all pathogens in such a way as to merely alter DNA adenine methylase

Art Unit: 1645

activity so to reduce a symptom in the subject and induce the desired protective immune response. The instant specification does not provide substantive evidence that the claimed vaccines are capable of inducing protective immunity when only a single symptom is reduced that is associated with infection. This demonstration is required for the skilled artisan to be able to use the claimed vaccines for their intended purpose of preventing or treating infections. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed vaccines, i.e. would not be able to accurately predict if protective immunity has been induced.

The mutant strain does not evidence a non-reverting mutation but may have any mutation that alters DNA adenine methylase activity for any period of time. A strain that reverts in vivo to a fully virulent pathogen, would not serve to induce a protective immune response and reducing a symptom associated with infection. Torreblance et al (1996) teaches that Dam mutant strains “are prone either to revert or to accumulate partial suppressors (page 23, col. 2, 1st paragraph).” Kupchella et al (1992, col. 1, page 33, second abstract) teaches various mutations that alter Dam adenine methylase activity that also evidence spontaneous reversions. With the prior art teaching the high frequency of reversion associated with mutations that alter adenine methylase activity, how will the mutant strain that has reverted reduce a symptom associated with infection? The revertant strains will cause infection and not serve the recited functional limitation of reducing symptoms to treat or prevent infection.

Art Unit: 1645

The ability to reasonably predict the capacity of a single bacterial immunogen to induce protective immunity from in vitro antibody reactivity studies is problematic. Ellis exemplifies this problem in the recitation that "the key to the problem (of vaccine development) is the identification of the at protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies"(page 572, second full paragraph). Unfortunately, the art is replete with instances where even well characterized antigens that induce an in vitro neutralizing antibody response fail to elicit in vivo protective immunity. See Boslego et al. wherein a single gonococcal pillin protein fails to elicit protective immunity even though a high level of serum antibody response is induced (page 212, bottom of column 2). Accordingly, the art indicates that it would require undue experimentation to formulate and use a successful vaccine without the prior demonstration of vaccine efficacy.

The specification fails to teach how and what genes in all of the pathogen chromosomes that will alter adenine methylase activity and would be capable of inducing an immune response that is protective. Further, the specification fails to provide an adequate written description of all the genes for all of the pathogens encompassed by the scope of the claims and all of the genes that would serve to alter DNA adenine methylase activity when mutated. The skilled artisan would be required to de novo locate, identify and characterize the claimed genes to be mutated and then to evaluate the strains for their ability to induce a protective immune response. This would require undue experimentation given the fact that the specification is completely lacking in teachings as to what genes would serve to alter DNA adenine methylase activity in all pathogens with the claimed

Art Unit: 1645

characteristics of being able to reduce a symptom associated with infection and also treat or prevent infection.

9. Claims 1-18, 20-23, 25-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites in the preamble the phrase “reducing virulence”, at line 3 of claim 1 the phrase “altering the bacteria’s native level of methylation” and on line 4, of claim 1 the phrase “inhibiting virulence”; the phrase “inhibiting virulence” lacks antecedent basis in the body and preamble of the claim. The recitation of differing terms which could have different meanings introduces a lack of clarity in the claim.

Claims 1-7 all recite an agent that “alters” the bacteria’s native level of DNA methyltransferase. Claims 2-4, 6 recite limitations directed to utilization of an agent that causes a reduction in bacteria’s native level of DNA methyltransferase while claims 5 and 7 recite claim limitations directed to utilization of an agent that causes an increase in bacteria’s native level of DNA methyltransferase. How can both an increase and a decrease in the bacteria’s native level of DNA methyltransferase result in reduction of bacterial virulence? Both an increase and a decrease would be an alteration in bacteria’s native level of DNA methyltransferase but both levels would not result in reduction of bacterial virulence unless the agent was specific for a specific virulence

Art Unit: 1645

component. The invention is not distinctly claimed based upon the recitation of contradictory claim limitations that do not recite any specific agent and level of alteration.

10. Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: providing a virulent bacteria that produces DNA methyltransferase activity, determining the native level of DNA methyltransferase activity in a bacteria.

11. Claim 8 recites the phrase "a Dam enzyme"; the recitation of the non-specific article "a", does not distinctly claim the invention. The phrase "a Dam enzyme" lacks antecedent basis in claim 1 which recites the phrase "DNA methyltransferase activity" and not the phrase --Dam enzyme--. The alteration effects the methyltransferase activity, and is not required in claim 1 to alter the Dam enzyme.

12. The terms " reduces or reducing or increases or decreases" recited in claims 2-18, 20-23, 25-28, 37-38 are relative terms which renders the claim indefinite. The term "reduces or reducing or increases" are not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

13. The terms "decreases and normal" in claim 9 are relative terms which render the claim indefinite. The terms "decreases and normal" are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art

Art Unit: 1645

would not be reasonably apprised of the scope of the invention. No specific bacteria are recited in the claim, no reference standard normal level is recited or determined in the claimed method relative to the required decrease; no means of comparison are provided in order to ascertain the decrease recited in claim 9.

Claim 9 recites the phrase “below a normal level”; this phrase lacks antecedent basis in claim 1 from which it depends which recite the phrase “native level”. Are the native and normal levels the same level? The normal level is not set forth in claim 9 to be the native level of the bacteria and is any level that could be asserted to be “normal”; the invention is not distinctly claimed.

Claims 11-18 recite the phrase “a pathogenic bacteria”; this phrase lacks antecedent basis in claim 1 which recites “reducing bacterial virulence”.

Claims 20 and 25 recite the phrase “level of expression of Dam”; the term “Dam” is the designator for a gene, while the base claim recites methyltransferase enzyme activity. The agent of claims 20 and 25 are not defined to be a gene specific agent; the combination of claim limitations are confusing in light of protein enzymatic activity being recited in the base claim, the nature and structure of the agent is not specifically defined and the recitation of a gene designator in the claim relative to its expression recites a combination of claim limitations that are not in agreement with each other.

Art Unit: 1645

Claims 21 and 26 recite the phrase “a Dam interaction site”; is this a protein or gene interaction site in light of the fact that “Dam” is a gene designator and the base claim recite protein enzymatic activity?

Claim 24 recites the phrase “a pathogenic bacteria”; the term “pathogenic” lacks antecedent basis in the preamble that recites “bacterial”; all bacteria that are present in a subject are pathogenic, (i.e. commensal bacteria). Clarification is requested.

Claim 24 recites the phrase “inhibits proliferation”; this phrase lacks antecedent basis in the preamble of the claim which recites the phrase “treating bacterial infection”.

Claim 28 recites in the preamble the phrase “treating bacterial infection”, as well as the phrase “inhibiting virulence”; the phrase “inhibiting virulence” lacks antecedent basis in the body and preamble of the claim. The recitation of differing terms which could have different meanings introduces a lack of clarity in the claim. Inhibition is a relative term which encompasses partial and full inhibition of virulence. Partial inhibition of virulence factor expression would not serve to treat or prevent infection, which it would only slightly reduce virulence factor expression. The combination of claim limitations recited in claim 28 do not correlate with the recited preamble which is directed to a method of treating infection, not just inhibiting virulence.

Claim 32 recites the phrases “treating bacterial infection”, “administering an agent” and “inhibiting the virulence of the bacteria”; but the composition was not administered to an infected person or animal, and the only living organism recited in the claim to which the agent was

Art Unit: 1645

administered is the bacteria and the bacteria is not infected with a bacterial infection. The claim is missing essential methods steps which would provide clarity to the claimed invention.

Claims 36-38, 40 recite the phrase "the agent" and depends from claim 34 which recites the term "compound". The term "agent" lacks antecedent basis in claim 34.

Claims 39-40 recite the phrase "wherein the bacteria is a pathogenic bacteria" and depends from claim 34 which recites the phrase "bacterial pathogenicity"; the term "bacteria" lacks antecedent basis in claim 34 which is directed to "pathogenicity" not bacteria.

Claims 17 and 45 and depend from claims 12 and 40, respectively and recite the phrase "selected from the group consisting of Shigella, Haemophilus, Bordetella, Neisseria, Pasteurella and Treponema". Claims 12 and 40 recite the phrase "selected from the group consisting of Escherichia, Vibrio, Yersinia and Salmonella"; claims 17 and 45 seek to broaden the scope of claims from which they depend. The members of the Markush group of claims 17 and 45 are not contained in the Markush group of claims 12 and 40, respectively. Claims 17 and 45 are confusing for reciting two Markush groups that are not overlapping at all.

Claim Rejections - 35 U.S.C. § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

Art Unit: 1645

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

15. Claims 1-2, 11-15, 17-18, 19 are rejected under 35 U.S.C. 102(e) as being anticipated by Vermeulen et al (US Pat. 5,872,104; filing date December 27, 1994).

(Instant claims 1,2, 6, 11-19,24,27) Vermeulen et al disclose the instantly claimed invention directed to a method of reducing bacterial (see col. 5, lines 15-24; bacteria include Staphylococcus spp., Croynebacterium, Bacteroides, Clostridium, Bacillus subtilis, Lactobacillus, Campylobacter, Propionibacterium spp., Mycoplasma spp, Fusobacterium, Veillonella, Streptococcus fecalis, Nocardia farcinica, Actinobacillus, Pseudomonas aeruginosa; Tables 6-7, col. 27-31 which includes Bordetella, Haemophilus, Neisseria meningitidis or gonorrhoeae) virulence (see column 19, lines 56-58; also see col. 5, lines 10-24; col. 13-15, E.coli, Pasteurella, Salmonella typhi, Yersinia, Shigella, Vibrio cholerae), the method comprising the step of:

contacting bacteria (col. 5, lines 10-24)

with an agent (see col. 39, lines 11-col. 46, especially col. 46, lines 5-17; col. 47, lines 25-43(inhibits DNA methylation); col. 5, lines 66-67; col. 5, lines 24-34, and especially col. 5, line 41 “6-methyladenine”; col. 5, lines 47-67; col. 6, lines 1-34),

Art Unit: 1645

that alters the bacteria's native level of DNA methyltransferase (Dam) activity (see col. 31, line 45 "SAM" is decreased(also see Figure 1A and Example VI, col. 56, lines 4-67); col. 2, lines 8-20; Figure 1A; col. 21, section B, starting at line 14; col. 22, line5; col. 59, Example VII).

With reduced substrate for methylase, through inhibition of SAM synthase, the native level of DNA methyltransferase activity (methylase, Fig. 1A) would be reduced.

(Instant claim 3, 9, 20,25, 32-33) Utilization of oligos, specifically 5' blocked oligodeoxynucleic acids, inhibition of translation of particular methylase mRNA can be inhibited (see col. 69, lines 60-67 and col. 70, lines 1-3; see all claims 1-132, especially claims 11, 27-28). Inhibition of SAM and SAH enzymes will lower the methylation of adenine (see col. 22, lines 1-20).

(Instant claim 4, 21, 23,26, 32-33) The utilization of adenosine analogues would block the Dam interaction site (see '10 4, claim 28).

(Instant claim 8): wherein the agent binds a Dam enzyme (see col. 22, line 5);

(Instant claims 24-27, 29-31, 32-33) Additionally, US Pat. 5,872,104, claims methods of treating a bacterial infection, the method comprising the steps of

Art Unit: 1645

administering to a subject infected with a pathogenic bacteria a therapeutically effective amount of a composition comprising a pharmaceutically acceptable carrier and an active agent that alters the bacteria's native level of DNA methyltransferase activity; and

allowing the agent to contact the bacteria for a period of time and under conditions so as to inhibit proliferation of the bacteria (see '104, claims 53-132).

(Instant claims 34-46) Another embodiment disclosed are compositions that comprise a carrier and a compound (see col. 70, lines 10-67 and col. 71-col. 78), wherein the compound is a methylation inhibitor (see col. 59, lines 20-54 and col. 77, line 67) and the carrier is a pharmaceutically acceptable carrier (liposomes/nanoparticles (see col. 75, lines 5-67), antibody targeting/carbohydrate targeting (see col. 76, lines 51-63), buffers and solutions (see col. 74, lines 46-67).

16. Claims 1, 5,7,10,19,22 (increased level of activity) are rejected under 35 U.S.C. 102(b) as being anticipated by Blyn et al (1990).

Blyn et al disclose the instantly claimed method of reducing bacterial virulence, the method comprising the step of:

contacting bacteria with an agent (the agent comprises pPY1025 and pTP166, see page 4049, col. 2, paragraph 4) that alters the bacteria's native level of DNA methyltransferase activity (3.5-fold higher levels of methylase activity and 69 fold increase with IPTG induction), wherein

Art Unit: 1645

the activity level is increased above the bacteria's native level (see page 4049, col. 2, paragraph 4, last two sentences).

Conclusion

17. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.
18. WO98/12206 is cited to show DNA adenine methyltransferases of several bacteria.
19. MacLeod (US Pat. 6,506,735 and 6,066,625) are cited to show compositions that comprise anti-sense compositions that inhibit DNA methyltransferase.
20. Torreblanca et al (1996, Genetics, Vol. 144) is cited to show live' attenuated pathogenic Salmonella strains that contain a mutation that alters the DNA adenine methylase activity of the strain such that it is attenuated (see abstract, first full sentence; page 20, col. 2, paragraph 3).
21. Radman et al (US Pat. 5,965,415) teach a mutated strain of Salmonella, wherein the mutation is in the mutL gene of Salmonella typhimurium resulting in an attenuated pathogenic strain of Salmonella that is non-toxic (col. 4, line 33) and suggests the use of the strain for inducing and eliciting an immune response to serve as a vaccine against Salmonellosis infection (col. 4, line 35) upon administration to an individual. The reference differs from the instantly claimed invention by failing to teach that a mutL mutation will alter DNA adenine methylase activity.
22. Ritchie et al (1988,1986) is cited to show strains of bacteria that evidence overproduction of DNA adenine methylase of 15 fold higher, 20-50 fold higher and 300-500 fold higher levels (see page 138, col. 2, paragraph 2).
23. Martin, C (1996); Brawer (ASM, abstract H-100, 1996); Rene et al (1988); Bandyopadhyay et al (1994; Vibrio dam gene cloned); Gunn et al (1997, shows damH of Neisseria gonorrhoeae); Lu et al (1990, mutB mutant Salmonella); Braaten, BA et al, pap pilus expression associated with dam methylase expression, 1991); Nou et al (1995, pili expression linked to dam, Lrp and Papi genes); Mankovich et al (1989, mutL is required for dam gene function); Meury, J et al (1995, shows various agents (hyper-osmotic shock, betaine) that effect bacterial cell conditions (see page 876, col. 2); Brawer et al (1998) is cited to show a temperature sensitive dam mutant of Salmonella typhimurium; vander Woude, MW et al (1994) is cited to show a dam mutant of

Art Unit: 1645

E.coli; Brooks et al (1983) is cited to show reduction and over expression of dam E.coli mutant strains (see introduction, page 837); Stambuk et al (1998) is cited to show interspecies recombination between E.coli and Salmonella typhimurium with respect to methylation; Guyot et al (1993) is cited to show site directed mutants of Dam methylase which lack catalytic activity (see abstract, page 3183); Stamm et al (1997) is cited to show a Treponema pallidum gene encoding DNA adenine methyltransferase; Marinus et al is cited to show an agent that reduces dam gene activity (insertion mutants).

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp
August 19, 2003


LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600